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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/652,864	08/29/2003	Heinz Kohler	200-019	1487

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EXAMINER	
TUNGATURTHI, PARITHOSH K	
ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/652,864	KOHLER ET AL.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *1-5 and 11-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/23/04;11/07/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group VI, claims 6-10 in the reply filed on 11/07/2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a)).

2. Claims 1-5 and 11-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions.

3. Claims 6-10 are under examination.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claim 6 is rejected under 35 U.S.C. 102(a) as being anticipated by Zhao[a] et al (J. Immunotherapy. 2002, 25:57-62; IDS – 11/07/2005).

Claims 6 is drawn to a method of producing an autophilic antibody by a chemical or genetic engineering techniques, wherein the autophilic antibody contains a T15 autophilic peptide having an amino acid sequence shown in SEQ ID NO:1 attached to the immunoglobulin component of the antibody

Zhao[a] et al teach the design and synthesis of self-binding (autophilic) antibodies (please see the materials and methods including the results section, in particular) wherein the T15 autophilic peptide was cross-linked to an anti-CD20 antibody. The T15 autophilic peptide utilized by Zhao et al is 100% identical to SEQ ID NO:1 of the instant application (please see page 58 column 1, under "Synthesis of Antibody-Peptide Conjugate" in particular).

Thus, Zhao[a] et al anticipate the instantly claimed autophilic antibody.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 6-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao[a] et al (J. Immunotherapy. 2002, 25:57-62; IDS – 11/07/2005) in view of Kohler et al (U.S Patent 6238667, Date Issued: May 29th, 2001) and Zhao[b] et al (J. Immunol. Methods. 2001. 254:137-145; IDS – 11/07/2005), Singh et al (U.S. Patent 7041459; Date Filed: May 21st 2002) and Rojas et al (Nature Biotechnology, 1998. 16:370-375).

Claim 6 has been described supra. Claims 7-10 are drawn to a method of producing an autophilic antibody by a chemical or genetic engineering techniques, wherein the autophilic antibody contains a T15 autophilic peptide having an amino acid sequence shown in SEQ ID NO:1 attached to the immunoglobulin component of the antibody, wherein the T15 peptide of the autophilic antibody is crosslinked to a nucleotide affinity site of the immunoglobulin, wherein the T15 peptide is crosslinked to a carbohydrate site of the Fc portion of the immunoglobulin, wherein the T15 peptide is

conjugated to an amino or sulfhydryl group of the immunoglobulin and wherein the autophilic antibody is expressed as a fusion protein containing the T15 autophilic sequence.

Zhao[a] et al has been described supra. Zhao[a] et al does not teach the different ways of cross-linking or conjugating the peptide to the antibody, these deficiencies are made up for by Kohler et al, Zhao[b] et al, Singh et al and Rojas et al.

Kohler et al teach a method of chemical cross-linking biologically active peptides to antibodies. Kohler, in particular, teach a method of affinity cross-linking a peptide to an antibody by photo-chemically activating an azido compound in a peptide including said azido compound; adding an antibody to the photochemically activated peptide; and allowing the photochemically activated peptide and the antibody to react. The azido compound has an affinity for a hydrophobic structure in the variable domain of the antibody which binds to nucleotides or nucleosides, binding the peptide into a native binding pocket of the immunoglobulin (Ig) structure of an antibody (abstract, in particular).

Zhao[b] et al teach the cross linking of MTS peptide to monoclonal antibodies via the carbohydrate moiety in the Fc domain of antibodies, without interfering with antigen recognition (please see discussion, in particular).

Singh et al teach that a peptide tag (e-tag for instance) can be covalently attached to sulfhydryl groups of the cysteine residues. In addition, Singh et al teach that such probes can be attached to the antibodies by reaction of the amino acid residues of

the antibody molecule, including the amine groups of lysine, the free carboxylic acid groups of glutamic and aspartic acid, the sulfhydryl groups of cysteine and the various moieties of the aromatic amino acids. The conjugation to an antibody may be random or site-directed. For site-directed conjugation the linker or mobility-modifying moiety may be joined in any convenient manner to a unit of the target-binding moiety, such as the Fc portion of an antibody or disulfides in the hinge region. For random conjugation amine groups (e.g., N-terminal or lysine) of the antibody may be employed. Alternatively, carboxylate groups (e.g., C-terminal, aspartic acid, glutamic acid) may be used. Other examples include thiol groups (please see paragraph 121, in particular).

Rojas et al teach the addition of a signal peptide to antibodies, which facilitated transmembrane transport, in addition to generating a fusion protein, which contained a 12-mer peptide (please see the entire document).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced the claimed method by combining the reference cited above.

One of ordinary skill in the art would have been motivated and would have reasonable expectation of success to have produced the claimed method because Zhao[a] et al teach the design of self-binding (autophilic) antibodies wherein the T15 autophilic peptide (that is 100% identical to the claimed SEQ ID NO:1) was cross-linked to an anti-CD20 antibody.

In addition, one of ordinary skill in the art would have been motivated and would have had a reasonable expectation of success to combine the teachings of Zhao[a] et al and Kohler et al because Kohler et al teach cross-linking biologically active peptides to antibodies, wherein photochemically activated peptide is allowed to react with an antibody, such that the peptide binds into a native binding pocket of the immunoglobulin structure of the antibody. Kohler teach that since the azido compound has an affinity for a hydrophobic structure in the variable domain of the antibody which binds to nucleotides or nucleosides, photochemically activating an azido compound in a peptide would render such peptide to be cross-linked to the nucleotide binding site of the antibody (please see the reference for a detailed mechanism of such binding properties).

Further, one of ordinary skill in the art would have known to combine the above teachings with those of Zhao[b] et al and Singh et al because Zhao[b] et al teach the cross linking of MTS peptide to monoclonal antibodies via the carbohydrate moiety in the Fc domain of antibodies, and Singh et al teach the covalent attachment of a peptide tag to sulfhydryl groups of the cysteine residues in an immunoglobulin molecule.

Thus, one of ordinary skill in the art would have been motivated and would have reasonable expectation of success to combine the above teachings and generate the claimed method of producing an autophilic antibody comprising all the limitations because Zhao[a] et al teach the design autophilic antibodies wherein the T15 autophilic peptide, which is 100% identical to the claimed SEQ ID NO:1, was cross-linked to an anti-CD20 antibody, and Kohler et al, Zhao[b] et al and Singh et al teach various methods

of cross-linking or conjugating a peptide to an antibody at various locations, and further because Rojas et al teach the production of a fusion protein comprising a antibody-peptide conjugate.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

9. No claims are allowed

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

11. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi, Ph.D.
Ph: (571) 272-8789

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER